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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/527,587 | 02/21/2006 | William E. Beschoner | 000241.00003 | 1006 |
| 22907 7590 04/01/2008 BANNER & WITCOFF, LTD. 1100 13th STREET, N.W. SUITE 1200 WASHINGTON, DC 20005-4051 | | | | |
| EXAMINER | | | | |
| SAJJADI, FEREDOUN GHOTB | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1633 | | | | |
| MAIL DATE | | DELIVERY MODE | | |
| 04/01/2008 | | PAPER | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/527,587

Applicant(s)

BESCHÖRNER ET AL.

Examiner

FEREYDOUN G. SAJJADI

Art Unit

1633

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 December 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 7-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/ISD)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date 3/14/2005

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicants' response of December 16, 2007, to the non-final action dated August 20, 2007 has been entered. Claims 1-12 are pending in the application. Claim 2 has been amended. No claims were cancelled or newly added. Claim 6 remains withdrawn from consideration, without traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Claims 1-5 and 7-12 are currently under examination.

Response to Information Disclosure Statement

Receipt of the references previously indicated as missing in the information disclosure statement filed 3/14/2005 is acknowledged. The references have been considered by the examiner and indicated as such on USPTO Form 1449.

Response to Objections to the Specification/Abstract

In view of the abstract having been provided on a separate sheet, apart from any other text, the previous objection is hereby withdrawn.

Response to Claim Rejections - 35 USC § 102

Claims 1, 2, 4, 5, 7 and 8 stand rejected under 35 U.S.C. §102(e) as being anticipated by Wu et al. (U.S. Patent No.: 6,995,299; filed Aug. 15, 2001). The rejection set forth on pp. 3-4 of the previous office action dated August 20, 2007 is maintained for reasons of record.

Applicants traverse the rejection, arguing that Wu does not teach a method of engrafting foreign replacement cells within a fetal non-human mammal comprising the steps recited in claim 1; and does not describe engrafting foreign replacement cells within a fetus. Rather, Wu describes inducing tolerance in a fetus and then "introducing human hepatocytes into the tolerized animal, preferably postnatally and preferably by intra-splenic injection, citing column

5, lines 6-8, and Example 10.1.4. Applicants' arguments have been fully considered, but are not found persuasive.

In response, it is noted that Applicants have based their arguments on selected teachings of Wu et al. that are directed to separate embodiments than those outlined in the previous office action. In column 5, the line preceding that quoted by Applicants states that the non-human animal is preferably a fetus or a neonate.

As previously indicated, the teachings of Wu et al. pertinent to the instant rejection are set forth in column 18, section 5.1.4, wherein Wu et al. state: "selection pressure may be used to favor the proliferation of human hepatocytes. Such selection pressure is defined herein as including any condition, preexisting in the host animal at the time of introduction of donor cells or imposed thereafter, which results in a greater likelihood that human hepatocytes, rather than host hepatocytes, will proliferate. For example, the selection pressure may result from the presence of a transgene that decreases the viability of host hepatocytes, either intrinsically (directly) or by administration of an activating agent (indirectly)... the transgene may be the albumin promoter/HSV-TK construct, whereby when gancyclovir is administered to the host animal (e.g., as an intraperitoneal injection of 250 mg/kg gancyclovir in sterile PBS), hepatocytes of the transgenic host may be selectively killed. In such embodiments, the death of host hepatocytes would be expected to favor compensatory proliferation of human hepatocytes." (column 18, lines 20-48). Thus, the human foreign replacement cells replace destroyed cells of the liver tissue (limitation of claim 1).

Therefore the rejection of claims 1, 2, 4, 5, 7 and 8 is maintained for reasons of record and the foregoing discussion.

Response to Claim Rejections - 35 USC § 103

Claims 1 and 3 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Wu et al. (U.S. Patent No.: 6,995,299; filed Aug. 15, 2001), in view of Loeb et al. (U.S. Patent No: 6,451,571; filed Sep. 17, 2002).

Claims 1 and 9-12 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (U.S. Patent No.: 6,995,299; filed Aug. 15, 2001), in view of Sorscher et al. (U.S. Patent No.: 6,017,896; filed Jun. 24, 1997).

The rejections set forth on pp. 4-7 of the previous office action dated August 20, 2007 are maintained for reasons of record.

Applicants traverse both rejections, arguing that Wu does not teach the step of implanting foreign replacement cells in the tissue of a fetal non-human mammal host. In fact, Wu teaches away from introducing foreign replacement cells in a fetus, because Wu teaches that the foreign replacement cells preferably are introduced postnatally, citing column 5, lines 6-8, and Example 10.1.4. Applicants' arguments have been fully considered, but are not found persuasive.

Applicants are directed to the response provided above. Wu et al. describe propagation of human hepatocytes in non-human animals, wherein said animals have chimeric livers, whereby some of substantially all of the hepatocytes present are human hepatocytes (Title and Abstract), and wherein the animal comprising human hepatocytes is preferably a fetus (column 5, line 5). Further, as stated in MPEP 2123, "[t]he prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

Applicants argue, nowhere does Loeb teach or suggest implanting foreign replacement cells in the tissue of the fetal non-human mammal host. Additionally arguing, nowhere does Sorscher teach or suggest implanting foreign replacement cells in the tissue of the fetal non-human mammal host. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is maintained that the implantation of human hepatocytes in the chimeric livers of recipient fetal animals is clearly taught by Wu et al. The secondary references of Loeb et al. and Sorscher et al. were cited to provide for the limitations of a mutated thymidine kinase; and immunoliposome mediated tissue-specific prodrug delivery, respectively.

Therefore the rejection of claims 1, 3 and 9-12 are maintained for reasons of record and the foregoing discussion.

Conclusion

Claims 1-5 and 7-12 are not allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREDYOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Art Unit: 1633

Fereydoun G. Sajjadi, Ph.D.

Examiner, Art Unit 1633

/Anne Marie S. Wehbe/

Primary Examiner, A.U. 1633